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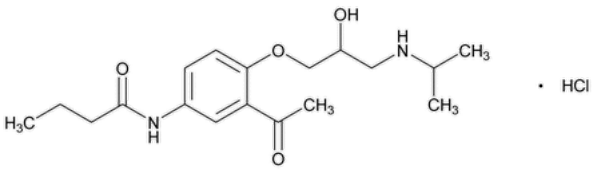
Acebutolol Hydrochloride



$C_{18}H_{28}N_2O_4 \cdot HCl$ 372.89

Butanamide, *N*-[3-acetyl-4-[2-hydroxy-3-[(1-methylethyl)amino]propoxy]phenyl]-, monohydrochloride, (±)-;

(±)-3'-Acetyl-4'-[2-hydroxy-3-(isopropylamino)propoxy]-butyranilide monohydrochloride CAS RN®: 34381-68-5; UNII: B025Y34C54.

DEFINITION

Acebutolol Hydrochloride contains NLT 98.0% and NMT 102.0% of acebutolol hydrochloride ($C_{18}H_{28}N_2O_4 \cdot HCl$), calculated on the dried basis.

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*:** 197K

• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

Change to read:

• **C. Identification Tests—General ⟨191⟩, *Chemical Identification Tests, Chloride*:** Meets the requirements of ▲the test for amine hydrochlorides▲ (USP 1-May-2021)

ASSAY

Change to read:

• **Procedure**

Mobile phase: Methanol, glacial acetic acid, and a 0.3% aqueous solution of sodium dodecyl sulfate (675:20:325) ▲▲ (USP 1-May-2021)

Standard solution: 0.14 mg/mL of USP Acebutolol Hydrochloride RS in water

Sample solution: 0.14 mg/mL of Acebutolol Hydrochloride in water

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 254 nm

Column: 3.9-mm × 30-cm; ▲10-µm▲ (USP 1-May-2021) packing L1

Flow rate: 2 mL/min

Injection volume: 10 µL

System suitability

Sample: *Standard solution*

Suitability requirements

▲▲ (USP 1-May-2021)

Tailing factor: NMT 2.5

Relative standard deviation: ▲NMT▲ (USP 1-May-2021) 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of acebutolol hydrochloride ($C_{18}H_{28}N_2O_4 \cdot HCl$) in the portion of Acebutolol Hydrochloride taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of acebutolol from the *Sample solution*

r_S = peak response of acebutolol from the *Standard solution*

C_S = concentration of USP Acebutolol Hydrochloride RS in the *Standard solution* (mg/mL)

C_U = concentration of Acebutolol Hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%

Change to read:

• **Organic Impurities**

Solution A: Mix 2.0 mL of phosphoric acid and 3.0 mL of triethylamine, and dilute with water to 1 L.

Solution B: Acetonitrile and *Solution A* (50:50)

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	98	2
2	98	2
30.5	10	90
41	10	90

Standard stock solution 1: 0.2 mg/mL of USP Acebutolol Related Compound A RS prepared as follows. Dissolve a suitable amount of USP Acebutolol Related Compound A RS in a suitable volumetric flask, in 50% of the total volume of acetonitrile, and dilute with *Solution A* to volume.

Standard stock solution 2: 0.2 mg/mL of USP Acebutolol Related Compound B RS prepared as follows. Dissolve a suitable amount of USP Acebutolol Related Compound B RS in a suitable volumetric flask, in 50% of the total volume of acetonitrile, and dilute with *Solution A* to volume.

Standard solution A: 0.002 mg/mL of USP Acebutolol Hydrochloride RS in *Solution A*

Standard solution B: 0.004 mg/mL of USP Acebutolol Related Compound I RS in *Solution A*

Standard solution C: 0.002 mg/mL of USP Acebutolol Related Compound A RS in *Solution A* from *Standard stock solution 1*

Standard solution D: 0.004 mg/mL of USP Acebutolol Related Compound B RS in *Solution A* from *Standard stock solution 2*

System suitability solution: 0.4 µg/mL each of USP Acebutolol Hydrochloride RS and USP Acebutolol Related Compound I RS in *Solution A* from *Standard solution A* and *Standard solution B*

Sample solution: 2 mg/mL of Acebutolol Hydrochloride in *Solution A*

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 240 nm

Column: 4.0-mm × 12.5-cm; 5-µm packing L1

Column temperature: 40°

Flow rate: 1.2 mL/min

Injection volume: 25 µL

System suitability

Samples: *Standard solution A* and *System suitability solution*

Suitability requirements

Resolution: NLT 7.0 between acebutolol and acebutolol related compound I, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution A*

Analysis

Samples: *Standard solution A*, *Standard solution B*, *Standard solution C*, *Standard solution D*, and *Sample solution*

Calculate the percentage of acebutolol related compound A, acebutolol related compound B, and acebutolol related compound I in the portion of Acebutolol Hydrochloride taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of acebutolol related compound A, acebutolol related compound B, or acebutolol related compound I from the *Sample solution*

r_S = peak response of acebutolol related compound A, acebutolol related compound B, or acebutolol related compound I from *Standard solution B*, *Standard solution C*, or *Standard solution D*

C_S = concentration of USP Acebutolol Related Compound A RS, USP Acebutolol Related Compound B RS, or USP Acebutolol Related Compound I RS in *Standard solution B*, *Standard solution C*, or *Standard solution D* (mg/mL)

C_U = concentration of Acebutolol Hydrochloride in the *Sample solution* (mg/mL)

Calculate the percentage of any unspecified impurity in the portion of Acebutolol Hydrochloride taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of any unspecified impurity from the *Sample solution*

r_S = peak response of acebutolol from *Standard solution A*

C_S = concentration of USP Acebutolol Hydrochloride RS in *Standard solution A* (mg/mL)

C_U = concentration of Acebutolol Hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 2*. ▲The reporting threshold is▲ (USP 1-May-2021) 0.05%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Acebutolol related compound B▲▲ (USP 1-May-2021)	0.72	0.2
Acebutolol related compound I▲▲ (USP 1-May-2021)	0.91	0.2
Acebutolol	1.00	—
Acebutolol related compound A▲▲ (USP 1-May-2021)	1.48	0.1
Any unspecified impurity	—	0.10
Total impurities[a]	—	0.5

[a] Total impurities include specified and unspecified impurities.▲▲ (USP 1-May-2021)

SPECIFIC TESTS

- **pH** ⟨791⟩

  Sample solution: 10 mg/mL of Acebutolol Hydrochloride in water

  Acceptance criteria: 4.5–7.0

- **Loss on Drying** ⟨731⟩

  Analysis: Dry at 105° for 3 h.

  Acceptance criteria: NMT 1.0%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers, and store at controlled room temperature.
- **USP Reference Standards** ⟨11⟩

  USP Acebutolol Hydrochloride RS

  USP Acebutolol Related Compound A RS

  N-(3-Acetyl-4-hydroxyphenyl)butyramide.

  $C_{12}H_{15}NO_3$ 221.25

  USP Acebutolol Related Compound B RS

  N-{3-Acetyl-4-[2-hydroxy-3-(isopropylamino)propoxy]phenyl}acetamide.

  $C_{16}H_{24}N_2O_4$ 308.37

  USP Acebutolol Related Compound I RS

  N-{3-Acetyl-4-[3-(ethylamino)-2-hydroxypropoxy]phenyl}butyramide.

  $C_{17}H_{26}N_2O_4$ 322.40

Topic/Question	Contact	Expert Committee
ACEBUTOLOL HYDROCHLORIDE	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

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